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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/679,664	10/03/2000	Thomas M. Stormann	072827-1801	7662

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EXAMINER	
LANDSMAN, ROBERT S	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 10/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/679,664	STORMANN ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 42-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 42-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Formal Matters

A. The Amendment filed 7/27/05 has been entered into the record.

B. Claims 1-11 and 42-62 are pending and are the subject of this Office Action. However, in the Amendment filed 7/27/05, no claim 62, along with the appropriate status identifier, has been listed.

C. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Declaration under 37 CFR 1.131

A. The Declaration submitted by Laura Storjohann with the Response filed 7/27/05 has been considered and is deemed persuasive regarding both 35 USC 101 and 35 USC 112, as seen below.

3. Claim Rejections - 35 USC § 101

A. The rejection of claims 1-11 and 42-62 under 35 USC 101 has been withdrawn in view of Applicants' arguments, as well as the Declaration submitted under 37 CFR 1.131 by Laura Storjohann.

4. Claim Rejections - 35 USC § 112, first paragraph - enablement

A. The rejection of claims 1-11 and 42-62 under 35 USC 112, first paragraph, has been withdrawn in view of Applicants' arguments, as well as the Declaration submitted under 37 CFR 1.131 by Laura Storjohann. As discussed above, the claimed invention possess utility under 35 USC 101.

B. The rejection of claims 1-11 and 42-62 under 35 USC 112, first paragraph, has been withdrawn in view of the Declaration under 37 CFR 1.131 by Laura Storjohann which states that intracellular domains with as few as 10 amino acid residues are functional.

C. Claims 1-11 and 42-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for full-length, wild-type, G protein fusion proteins coupled to a promiscuous G protein, does not reasonably provide enablement for G protein fusion proteins which are "at least 75% identical to" specific receptor sequences. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The Examiner notes that this rejection was previously made in the Office Action mailed 4/29/04 and withdrawn in the Action mailed 1/24/05 in view of Applicants' arguments filed 10/29/04. However, upon further consideration, the rejection is being reinstated.

First, the breadth of the claims is excessive with regard to claiming all fusion proteins which comprise various regions of CaR, mGluR and GABAR which are less than the full-length receptors (i.e. "**at least 75% identical**"). Proteins which are "at least 75% identical" to these wild-type proteins would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the full-length proteins.

Applicants provide no guidance or working examples of proteins which are at least 75% identical to CaR, mGluR or GABAR. Applicants have provided no guidance as to what critical residues are required to maintain the functional characteristics of these proteins. Furthermore, it is not predictable to one of ordinary skill in the art how to make a functional CaR, mGluR or GABAR protein which is less than 100% identical to that the wild-type, especially when producing fusion proteins (chimeras) of these proteins. Applicants have previously argued that the Examiner has not provided any support for his position other than assertions.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene.

Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene

superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. Finally, Wells teaches that even a single substitution of Alanine into a protein can have profound effects on a protein's function (page 1081; 3rd column).

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan the utility of the claimed polynucleotides

In summary, the breadth of the claims is excessive with regard to Applicants claiming all CaR, mGLuR and GABAR which are at least 75% identical to the wild-type protein. There is also a lack of guidance and working examples of these proteins as well as which residues are critical for protein function. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make a functional protein other than that of the wild-type, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

5. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 1-11 and 42-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Proteins which are "at least 75% identical" to these wild-type proteins would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the full-length proteins.

The scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art

do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "CaR, mGluR and GABAR alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

6. Conclusion

A. No claim is allowed.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (571) 272-0888. The examiner can normally be reached on T-F 10 AM – 7 PM (eastern).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert Landsman
Primary Examiner
Art Unit 1647